Kinetics of Complexation between β-Cyclodextrin and 1-Propanol in Aqueous Solution by Ultrasonic Relaxation Method

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Ultrasonic absorption coefficients in aqueous solutions containing β-cyclodextrin and alcohols (ethanol and 1-propanol) have been measured in the frequency range from 3 to 220 MHz at 25 °C. Although a single relaxational absorption has been observed in solution with β-cyclodextrin and 1-propanol, it has not been found when the alcohol is ethanol. From the concentration dependence of the ultrasonic relaxation parameters, the cause of the relaxational absorption has been attributed to the perturbation of an equilibrium associated with the 1 : 1 complex formation (complexation) between β-cyclodextrin and 1-propanol. The rate and equilibrium constants as well as the standard volume change were determined for the complexation reaction of β-cyclodextrin and 1-propanol. The equilibrium constant determined in this study was found to be very consistent with the reported value for β-cyclodextrin and 1-propanol. The kinetic process for complexation between β-cyclodextrin and popular alcohols is discussed in relation to the sizes of the guest molecules.

It is well known that the structures and thermodynamic stabilities of the host–guest complexes formed by cyclodextrins and additives vary with the nature of the cyclodextrin and guests.[1] It is said that the complexes are created through hydrophobic interaction, Van der Waals interaction, or hydrogen bonding. Therefore, the reaction rate associated with the complexation process is strongly dependent on the conditions of the host and guest molecules,[2] i.e. the sizes, the hydrophobicities, and the ionic conditions. In order to examine further how fast the complexation process occurs and how the size of the guest molecules affects on the kinetics, we have considered that alcohols may be appropriate as the guest molecules, because it is possible to estimate their hydrophobicity; also the conditions for ionic species do not need to be considered. Although the equilibrium constants for complexation between cyclodextrins and nonelectrolytes have been determined by many investigators,[3—6] kinetic studies concerning complexation with nonelectrolytes have so far been very scarce. However, kinetic information is very important in applications of host–guest complexes, such as separation technology and drug delivery systems.

The ultrasonic relaxation method may provide useful information concerning fast reactions which occur in liquids and solutions. The present authors have been utilizing this method to investigate fast reactions in aqueous solutions.[7—9] Especially, a recently constructed ultrasonic resonator[10] has enabled us to measure the ultrasonic absorption coefficients over a wide frequency range down to 3 MHz, which may provide more accurate ultrasonic relaxation parameters.

Under these situations, we have wished to study systematically reaction kinetics concerning the host–guest complex. For this purpose, at the first stage, β-cyclodextrin and two alcohols were chosen as the host and guest, respectively, and the ultrasonic relaxation method was applied in order to obtain the fast kinetic data for the complexation.

Experimental

β-Cyclodextrin, ethanol, and 1-propanol were purchased from Wako Pure Chemicals Co., Ltd. They were used without further purification. A thermogravimetric analysis for β-cyclodextrin was carried out in order to determine the content of water in the purchased chemical (proved to be as 10.97 wt%); the result was taken account for preparing sample solutions. The desired aqueous solutions were prepared by weighing, using distilled and filtered water through a MilliQ SP-TOC system from Japan Millipore Ltd. The sample solutions were left for at least one day before measurements.

The ultrasonic absorption coefficients, α, were obtained by a pulse method in the frequency range from 15 to 220 MHz and by a resonance method from 3 to 6 MHz. The details concerning the apparatus and measurement procedures have been described elsewhere.[10,11] The mechanical loss of the resonator could be determined from the results in liquid water, since the acoustic impedance for the solution is almost the same as that of the solvent. Sound velocity and density measurements were carried out using a sing-around meter at 1.92 MHz and a vibration density meter, respectively. The measurement temperature was 25 °C.

Results and Discussion

Figures 1 and 2 show the frequency dependence of the absorption coefficient divided by the square of the measurement frequency, α/f^2, for an aqueous solution of β-cyclodextrin as well as for those also including alcohols, where f is the measurement frequency. As can be seen, no relaxational absorption can be observed in the solution of β-cyclodextrin, the result of which is consistent with that reported by Rohrbach et al.[12] A slight increase of α/f^2 in a lower frequency range below 10 MHz in not regarded as indication of the excess absorption, but, rather an experimental error. The addition of 1-propanol caused a clear appearance of relaxational ab-

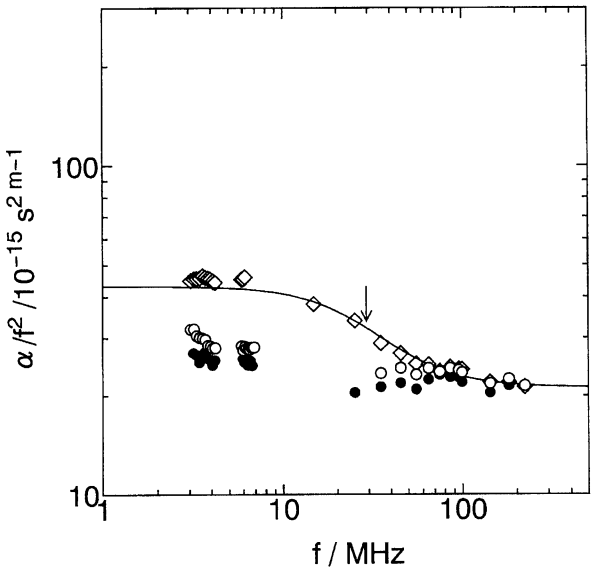

Fig. 1. The representative ultrasonic absorption spectra in aqueous solutions of β-cyclodextrin and alcohols at 25 °C. ●: 0.0111 mol dm^{-3} β-cyclodextrin, ○: 0.0111 mol dm^{-3} β-cyclodextrin and 0.300 mol dm^{-3} ethanol, ◇: 0.0111 mol dm^{-3} β-cyclodextrin and 0.140 mol dm^{-3} 1-propanol.

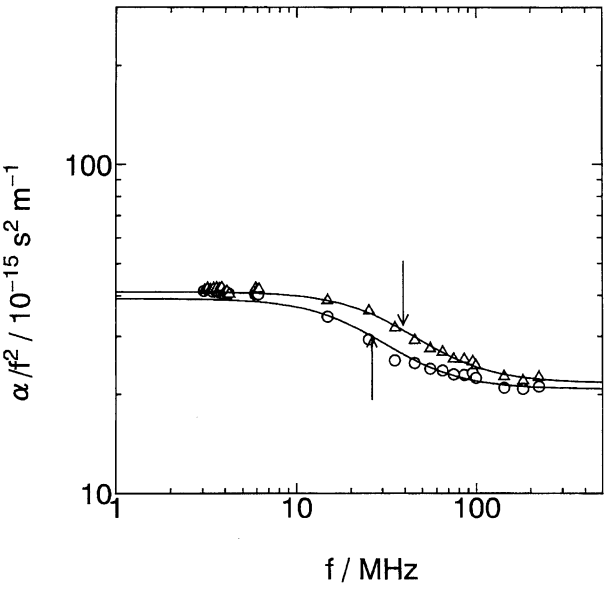

Fig. 2. The ultrasonic absorption spectra in aqueous solution of β-cyclodextrin at 0.0111 mol dm^{-3} with 1-propanol. ○: 0.05 mol dm^{-3}, △: 0.300 mol dm^{-3} of 1-propanol.

sorption, while no relaxation was not found in the frequency range form 3 to 220 MHz when ethanol was used as the additive. Actually, relaxational absorption is surely observed in concentrated aqueous solutions of 1-propanol.[13,14] However, the 1-propanol concentrations used in this study were too low and no relaxational absorption was observed at such low concentrations. It is therefore certain that the observed relaxational absorption is responsible for β-cyclodextrin and 1-propanol. The frequency dependence of α/f^2 in a solution containing 1-propanol was tested as to whether it may fit to the usual Debye-type single relaxational equation,

$$\alpha/f^2 = A/[1+(f/f_r)^2]+B, \quad (1)$$

where f_r is the relaxation frequency, and A and B are the constants. These ultrasonic parameters, f_r, A, and B, were determined so as to obtain the best fit of the experimental data to Eq. 1 using a nonlinear least-mean square method. The observed spectra were found to agree with the single relaxational equation, as can be seen in Figs. 1 and 2. Thus, the determined ultrasonic parameters are listed in Table 1 along with the values of the sound velocity, c, and density, ρ.

According to several investigations[3,4] carried out previously using static experimental methods, it has been said that alcohols form 1 : 1 complex with β-cyclodextrin. The complexation equilibrium is simply expressed as

$$\mathrm{CD + ROH} \underset{k_b}{\overset{k_f}{\rightleftharpoons}} \mathrm{CDROH}, \quad (2)$$

where CD is β-cyclodextrin, ROH alcohol, and CDROH the complex. The forward and backward rate constants are indicated by k_f and k_b, respectively.

Following the analytical procedure of the relaxation method, the relaxation frequency is related to the rate constants and the reactant concentrations as follow:[15]

$$2\pi f_r = k_f([\mathrm{CD}]+[\mathrm{ROH}])+k_b. \quad (3)$$

The activity coefficients for the reactants were assumed to be unity, because the concentrations of the reactants were not very high. The above relation may be expressed in terms of the analytical concentrations of β-cyclodextrin, C_{dx}, and alcohol, C_{al}, to give

Table 1. Ultrasonic Relaxation Parameters, Sound Velocity, and Density for Aqueous Solution of β-Cyclodextrin and 1-Propanol at 25 °C

Concn		f_r	A	B	c	ρ
C_{dx}	C_{al}					
mol dm^{-3}		MHz	10^{-15} s^2 m^{-1}		m s^{-1}	kg dm^{-3}
0.0111	—	—	—	21.7±0.6	1495	1.0036
0.0111	0.0500	26±2	18±1	20.8±0.1	1499	1.0029
0.0111	0.0802	27±2	23±1	21.0±0.1	1499	1.0028
0.0111	0.0999	25±1	25±1	21.2±0.1	1501	1.0024
0.0111	0.140	29±2	22±2	21.2±0.1	1502	1.0020
0.0111	0.150	31±1	22±1	21.2±0.1	1502	1.0019
0.0111	0.200	35±2	24±1	20.8±0.1	1510	1.0017
0.0111	0.250	39±3	19±2	21.2±0.2	1508	1.0006
0.0111	0.300	39±2	19±1	21.7±0.1	1510	1.0011
0.0111	0.389	57±3	17±1	20.7±0.1	1516	1.0003
0.0111	0.500	58±2	15±1	21.0±0.1	1520	0.9984
0.0178	0.140	28±2 (31.0)	39±3	21.3±0.1	1503	—
0.0178	0.200	34±2 (35.6)	33±2	21.6±0.1	1505	—
0.0178	0.300	40±2 (43.4)	28±1	21.7±0.1	1510	—
0.00556	0.200	29±2 (35.5)	22±2	21.3±0.1	—	—

$$2\pi f_r = k_b[\{1 + K(C_{dx} + C_{al})\}^2 - 4K^2 C_{dx} C_{al}]^{1/2}, \quad (4)$$

where K is the equilibrium constant defined as $K = k_f/k_b$. At a fixed concentration of β-cyclodextrin, $C_{dx} = 0.0111$ mol dm^{-3}, the 1-propanol concentration dependence of the relaxation frequency was examined to satisfy the experimental data with Eq. 4, using a nonlinear least-mean square method. When $k_b = (1.21 \pm 0.07) \times 10^8$ s^{-1} and $K = 4.2 \pm 0.6$ mol^{-1} dm^3, a minimum standard deviation is obtained. Rekharsky et al.[4] have reported to be $K = 4.5 \pm 1.7$ mol^{-1} kg using titration calorimetry, and $K = 3.72$ mol^{-1} dm^3 has been found by Matsui and Mochida[3] through a spectrophotometric examination. It can be seen that the result obtained kinetically in this study is very close to the literature values, because the solution density is almost the same as that of solvent water. The forward rate constant was then obtained to be $k_f = (5.1 \pm 0.7) \times 10^8$ mol^{-1} dm^3 s^{-1} based on the definition of the equilibrium constant.

The absorption measurements at different β-cyclodextrin concentrations were also carried out, the results of which are shown in Table 1. Since the rate and equilibrium constants are now known, it is possible to calculate the relaxation frequency at different concentrations using Eq. 4. The calculated relaxation frequencies are indicated in the parenthesis in Table 1. They are close to the experimentally determined values. Figure 3 shows the results of the concentration dependence of the relaxation frequency multiplied by 2 π at various conditions for β-cyclodextrin and 1-propanol. All of the relaxation frequencies obtained fall on a single line, the result of which confirms that the observed relaxational absorption is due to the complexation process.

The maximum absorption per wavelength, μ_{max}, is also obtainable from the absorption measurement along with the sound velocity and density. It is given by the following equation under an assumption of the volume relaxation, which is reasonable for aqueous solution:

$$\mu_{max} = 0.5 A f_r c = \pi \rho c^2 (1/[CD] + 1/[ROH] + 1/[CDROH])^{-1} (\Delta V)^2 / 2RT. \quad (5)$$

Here, ΔV is the standard volume change in the reaction. The determined volume change using above relation has been proven to be concentration independent, giving $(12.5 \pm 0.3) \times 10^{-6}$ m^3 mol^{-1} for the complexation between β-cyclodextrin and 1-propanol.

Gramer et al.[2] have examined the reaction kinetics for the complexation of α-cyclodextrin with nitrophenol and azo dyes. The complexation rate constants have been found to be dependent on the conditions of the guest molecules. From a kinetic specificity with respect to the guest molecules, they proposed the probable reaction mechanisms of the formation of the inclusion compound to be: 1) a breakdown of the water structure around guest molecule which is going to be included in the host, and transport of some water molecules into the solution, and 2) an interaction between the substituents of the guest molecule and the host molecule on the rim or on the inside of the host. It may be certain that alcohol molecules are included in the cavity of cyclodextrin. From the fact that ultrasonic relaxation is observed in a solution with 1-propanol, and that it is not found in a solution with ethanol, it is speculated that the hydrophobic interaction is important for the complexation between β-cyclodextrin and alcohols. Along with an increase in the hydrophobicity of the guest molecules, the forward and/or backward rate constants are expected to be diminished, because of the hydrophobic interaction between the host and guest molecules. It is considered that some water molecules exist in the cavity, and that they may be transported to the bulk solution when the guest is included. This may correspond to mechanism 1). Inside the cavity, an alcohol molecule could be stabilized by the hydrophobic interaction when the hydrophobicity of alcohol is relatively high. This causes a stabilization of the host–guest complex. It is therefore expected that both of the proposed two mechanisms are dominant for the complexation of alcohol. Thus, the small volume change of the reaction may be understood to imply that the transport of some water molecules in the cavity of the host into the bulk solution compensates with the inclusion of 1-propanol into the cavity of the host.

The equilibrium constant for β-cyclodextrin and ethanol is reported to be 0.933 mol^{-1} dm^3.[3] It is thus possible to estimate the relaxation frequency; for example, at $C_{al} = 0.300$ mol dm^{-3} of ethanol with 0.0111 mol dm^{-3} of β-cyclodextrin, because the relation, $2\pi f_r = 1.3 k_f$, is obtained. Therefore, even if the forward rate constant were similar for different alcohols, the relaxation process would exist in a higher frequency range than that used in this study.

In order to specify further the kinetic behaviors for the complexation of nonelectrolytes into the guest cavities, it is

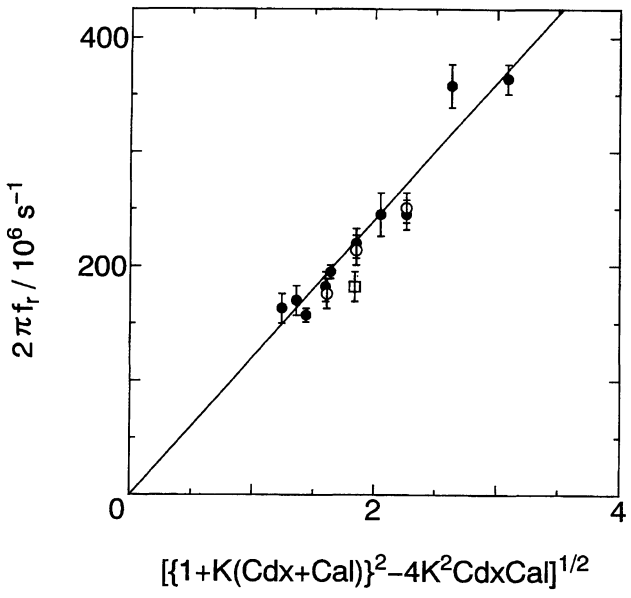

Fig. 3. The concentration dependence of the relaxation frequency for aqueous solution of β-cyclodextrin with 1-propanol. ●: 0.0111 mol dm^{-3}, ○: 0.0178 mol dm^{-3}, □: 0.00556 mol dm^{-3} of β-cyclodextrin.

necessary to accumulate more experimental data for various alcohols and cyclodextrins.

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